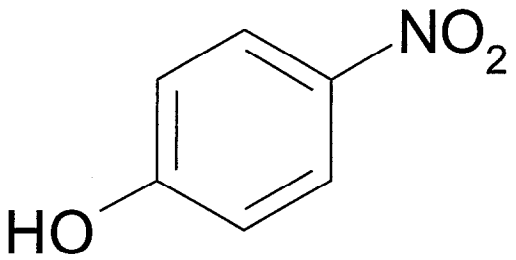
p-Nitrophenol (CASNO 100-02-7)



U.S. EPA HPV

Data Set

Existing Chemical	:	ID: 100-02-7
CAS No.	:	100-02-7
EINECS Name	:	4-nitrophenol
EC No.	:	202-811-7
TSCA Name	:	Phenol, 4-nitro-
Molecular Formula	:	C6H5NO3

Producer related part

Company	:	Solutia Inc
Creation date	:	10.02.2004

Substance related part

Company	:	Toxicology and Regulatory Affairs
Creation date	:	10.02.2004
Status	:	
Memo	:	Revised Robust Summaries
Printing date	:	29.02.2004
Revision date	:	
Date of last update	:	29.02.2004
Number of pages	:	29

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	manufacturer
Name	:	Solutia Inc
Contact person	:	
Date	:	
Street	:	
Town	:	
Country	:	
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	
Remark	:	Updated February 2004 by Elmer Rauckman PhD DABT Toxicology and Regulatory Affairs Freeburg, IL rauckman@toxicsolutions.com

29.02.2004

1.2 SYNONYMS AND TRADENAMES

2.1 MELTING POINT

Value	:	= 114 °C
Sublimation	:	
Method	:	other
Year	:	1996
GLP	:	no data
Test substance	:	no data
Reliability	:	(2) valid with restrictions Cited as a Peer reviewed reference in HSDB (2002) for 4-nitrophenol; also cited as a definitive value in IPCS CICAD Document 20 - Mononitrophenols (2000).
Flag	:	Critical study for SIDS endpoint

24.10.2002 (4)

2.2 BOILING POINT

Value	:	> 279 °C at
Decomposition	:	Yes
Method	:	other
Year	:	1987
GLP	:	no data
Test substance	:	no data
Test substance	:	p-Nitrophenol CASNO 100-02-7
Reliability	:	(2) valid with restrictions Handbook values are assigned a reliability score of 2
Flag	:	Critical study for SIDS endpoint

24.10.2002 (13)

2.4 VAPOUR PRESSURE

Value	:	= .00013 hPa at 20 °C
Decomposition	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	
Remark	:	Vapor pressure converted to hPa from original extrapolated 20 deg value of 1.27 exp -7 Atm.
Test substance	:	p-Nitrophenol CASNO 100-02-7
Reliability	:	(2) valid with restrictions Data obtained by a scientifically defensible method.
Flag	:	Critical study for SIDS endpoint

19.02.2004 (16)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	
Log pow	:	<= 1.91 at °C
pH value	:	
Method	:	other (calculated)
Year	:	1985
GLP	:	no data
Test substance	:	no data
Source	:	Solutia Inc. St. Louis
Reliability	:	(2) valid with restrictions Value of <2.4 cited as definitive value in IPCS CIDAD Document 20 - Mononitrophenols (2000).
Flag	:	Critical study for SIDS endpoint

24.10.2002 (8)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	
Value	:	= 16000 mg/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other
Year	:	1996
GLP	:	no data
Test substance	:	no data
Reliability	:	(2) valid with restrictions Cited as a Peer reviewed reference in HSDB (2002) for 4-nitrophenol.
Flag	:	Critical study for SIDS endpoint

24.10.2002 (23)

3.1.1 PHOTODEGRADATION

Type	:	other: Air and water
Light source	:	Sun light
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Spectrum of substance	:	lambda (max, >295nm) : 290 nm epsilon (max) : epsilon (295) :
Conc. of substance	:	10 mol/l at °C
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= 6.7 day(s)
Degradation	:	% after
Quantum yield	:	
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000
Rate constant	:	= .0000000000043 cm^3/(molecule*sec)
Degradation	:	= 50 % after 2.5 hour(s)
Deg. product	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	

Method :

DIRECT:
Dissolved in deionized water (1.18 g/100 ml) to which was added an acetate, phosphate or borate component to bring solution to pH 5, 7 or 9, respectively and introduced to sunlight (blind controls used). Analysis performed by GC using EC detector.

INDIRECT:
The indirect photolysis rate and half-life were estimated using the Atmospheric Oxidation Program for Microsoft Windows (AOPWIN ver 1.90) that estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. This program uses structural features of the molecule to estimate and sum the individual contribution of each hydrogen atom to arrive at a reaction-rate constant for hydrogen abstraction by atmospheric hydroxyl radical. It also estimates the rate constant for the gas-phase reaction between ozone and olefinic or acetylenic compounds. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon average atmospheric concentrations of hydroxyl radicals and ozone.

Remark :

The directphotolysis estimate is based on aqueous solutions in direct sunlight and although the half-life is longer than for atmospheric material it can be an important mechanism for PNP loss because PNP has such low volatility/

Result :

The following results are from APOWIN based on the structure of the molecule

```
AOP Program (v1.90) Results:
============================
SMILES : c1cc(O)ccc1N(=O)(=O)
CHEM   :
MOL FOR: C6 H5 N1 O3
MOL WT : 139.11
----- SUMMARY (AOP v1.90): HYDROXYL RADICALS ----------
----
Hydrogen Abstraction       =   0.0000 E-12
cm3/molecule-sec
Reaction with N, S and -OH =   0.1400 E-12
cm3/molecule-sec
Addition to Triple Bonds   =   0.0000 E-12
cm3/molecule-sec
Addition to Olefinic Bonds =   0.0000 E-12
cm3/molecule-sec
Addition to Aromatic Rings =   4.1652 E-12
cm3/molecule-sec
Addition to Fused Rings    =   0.0000 E-12
cm3/molecule-sec

   OVERALL OH Rate Constant =   4.3052 E-12
cm3/molecule-sec
   HALF-LIFE =     2.484 Days (12-hr day; 1.5E6 OH/cm3)
   HALF-LIFE =    29.813 Hrs

---- SUMMARY (AOP v1.90): OZONE REACTION --------------
----

       ******  NO OZONE REACTION ESTIMATION ******
       (ONLY Olefins and Acetylenes are Estimated)

 NOTE: Reaction with Nitrate Radicals May Be Important

Experimental Database:  NO Structure Matches
```

Test substance :
p-Nitrophenol CASNO 100-02-7

Conclusion :
Indirect photolysis in atmosphere: Half-life = 2.5 days

Direct photolysis in water: Half-life of 5.7 days at pH of 5, 6.7 days at pH of 7 and 13.7 days at pH 9.

Reliability : (2) valid with restrictions
Estimates based on EPIWIN are assigned a reliability of 2.

Flag : Critical study for SIDS endpoint

20.02.2004 (3) (11)

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Degradation : < 50 % after 1 year at pH and °C

Method :

The water stability of this material may be reliably estimated from chemical principles. Aromatic nitro groups and hydroxyl groups are listed as functional groups that are generally resistant to aqueous hydrolysis at environmental pH levels (Harris 1990).

In addition to hydrolytic stability the effect of sunlight on environmental fate in surface waters is a factor needs to be considered for this compound. Hustert, et al (1981) determined the effect of natural sunlight on PNP in water at three different pH values. They found that sunlight exposure caused loss of PNP with a half-life of about a week (please see the accompanying robust summary on photodegradation for details)

(Hustert, K,, Mansour, M, Parlar, H and Korte, F. 1981. Der EPA-Test - Eine methode zur bestimmung des photochemischen abbaus von organischen verbindungen in aquatischen systemen. Chemosphere 10 (9):995-998.)

Result :

The knowledge that the functional groups in PNP are not susceptible to hydrolysis allows prediction of a half-life > 1 year for PNP in the absence of significant exposure to direct sunlight. In situations where the compound is exposed to direct sunlight by presence in the first few cm of surface water, the half-life will be shorter proportionally to the sunlight exposure.

Test substance :

p-Nitrophenol CASNO 100-02-7

Conclusion :

The hydrolysis half-life of PNP at ambient temperatures and typical environmental pH levels is greater than one year. Exposure of PNP containing surface water to direct sunlight will cause loss of PNP with a half-life of about a week.

Reliability : (2) valid with restrictions

A reliability code of 2 is assigned to values obtained from reliable estimation methods.

Flag : Critical study for SIDS endpoint

19.02.2004 (9)

3.3.2 DISTRIBUTION

Media : other: air, water, soil, sediment
Method : Calculation according Mackay, Level III
Year : 2004

Method :

Measured values for physical values of PNP were input into EPIWIN as shown below. Biodegradation rates were estimated from experimental results showing inherent biodegradability. Model was set to assume initial distribution to water only as this is the most likely industrial situation. EQC Level III model (as found in EPIWIN 3.05) was utilized.

Result : Results of the Level III fugacity modeling are:

Level III Fugacity Model (Full-Output):

Chem Name : 4-Nitrophenol
Molecular Wt: 139.11
Henry's LC : 4.15e-010 atm-m^3/mole (user-entered)
Vapor Press : 9.79e-005 mm Hg (user-entered)
Liquid VP : 0.000743 mm Hg (super-cooled)
Melting Pt : 114 deg C (user-entered)
Log Kow : 1.91 (user-entered)
Soil Koc : 33.3 (calc by model)

	Concentration (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	7.18e-008	55	0
Water	99.8	360	1000
Soil	0.000177	360	0
Sediment	0.187	500	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	4.31e-019	3.09e-6	2.46e-6	3.09e-7	2.46e-007
Water	5.09e-015	658	342	65.8	34.2
Soil	9.1e-020	0.00116	0	0.000116	0
Sediment	2.65e-015	0.886	0.0128	0.0886	0.00128

Persistence Time: 342 hr
Reaction Time: 520 hr
Advection Time: 1e+003 hr
Percent Reacted: 65.8
Percent Advected: 34.2

Half-Lives (hr), (based upon user-entry):
Air: 55
Water: 360
Soil: 360
Sediment: 500

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

Test substance :

p-Nitrophenol CASNO 100-02-7

Conclusion :

Under conditions of initial distribution to water, PNP is expected to remain almost exclusively in the water compartment with less than 0.2% predicted to distribute to sediment.

Reliability : (2) valid with restrictions

A reliability code of 2 is assigned to values obtained from reliable estimation methods.

Flag : Critical study for SIDS endpoint

19.02.2004 (14)

3.5 BIODEGRADATION

Type : aerobic
Inoculum :
Concentration : 1 mg/l related to DOC (Dissolved Organic Carbon)

Contact time : 30 day(s)
Degradation : = 0 % after 30 day(s)
Result : under test conditions no biodegradation observed

Method :

Closed bottle test, after OECD 301D

Test substance :

p-Nitrophenol CASNO 100-02-7

Reliability : (2) valid with restrictions

Details lacking.

Flag : Critical study for SIDS endpoint

29.02.2004 (6)

Type : aerobic
Inoculum :
Concentration : 50 mg/l related to DOC (Dissolved Organic Carbon) related to
Contact time : 14 day(s)
Degradation : 1 % after 14 day(s)
Result : under test conditions no biodegradation observed

Method :

Followed MITI protocol except innoculum collected from several sites in the area of the laboratory.

Test substance :

p-Nitrophenol CASNO 100-02-7

Reliability : (2) valid with restrictions

Details lacking

29.02.2004 (6)

Type : aerobic
Inoculum :
Concentration : 1 mg/l related to DOC (Dissolved Organic Carbon) related to

Contact time	:	30 day(s)
Degradation	:	= 60 % after 30 day(s)
Result	:	other: limited biodegredation under conditions
Method	:	Modified closed bottle test, similar to OECD 301D
Remark	:	Modified conditions included some trace matals and vitamins added to medium.
Test substance	:	p-Nitrophenol CASNO 100-02-7
Reliability	:	(2) valid with restrictions Details lacking.

29.02.2004 (6)

Type	:	aerobic
Inoculum	:	
Concentration	:	10 mg/l related to DOC (Dissolved Organic Carbon) related to
Contact time	:	28 day(s)
Degradation	:	90 % after 28 day(s)
Result	:	inherently biodegradable
Method	:	Used standard Sturm test procedure as described by Sturm (1973) with carbon dioxide evolution as the measured indicator of biodegradation.
Remark	:	Standard Sturm test
Test substance	:	p-Nitrophenol CASNO 100-02-7
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.02.2004 (6)

Type	:	aerobic
Inoculum	:	
Concentration	:	400 mg/l related to DOC (Dissolved Organic Carbon) related to
Contact time	:	10 day(s)
Degradation	:	92 % after 10 day(s)
Result	:	inherently biodegradable
Method	:	Followed procedure of Zahn and Wellens except that only DOC was measured.
Test substance	:	p-Nitrophenol CASNO 100-02-7
Reliability	:	(2) valid with restrictions Details lacking

29.02.2004 (6)

Type : aerobic
Inoculum :
Concentration : 40 mg/l related to DOC (Dissolved Organic Carbon)
related to
Contact time : 42 day(s)
Degradation : 97 % after 42 day(s)
Result : readily biodegradable

Method :
Standard French norm procedure (ANFOR)
Test substance :
p-Nitrophenol CASNO 100-02-7
Reliability : (2) valid with restrictions

Details lacking
29.02.2004 (6)

Type : aerobic
Inoculum :
Contact time : 19 day(s)
Degradation : 100 % after 19 day(s)
Result : readily biodegradable

Method :
Modeled after OECD sceeening test except some trace minerals and viatamins were added to enhance bacterial activity. Prodedure modified to use DOC analysis as measured parameter. COncentration 20 or 10 mg C/L.
Test substance :
p-Nitrophenol CASNO 100-02-7
Reliability : (2) valid with restrictions

Details lacking
29.02.2004 (6)

Type : aerobic
Inoculum :
Concentration : 10 mg/l related to DOC (Dissolved Organic Carbon)
related to
Contact time : 42 day(s)
Degradation : 100 % after 42 day(s)
Result :

Method :
Modified Sturm test with preacclimation procedure with 20 mg/l test material. Prodedure modified to use DOC for measurement.
Remark :
Modified Sturm test
Test substance :
p-Nitrophenol CASNO 100-02-7
Reliability : (2) valid with restrictions

Details lacking

29.02.2004 (6)

Type	:	aerobic
Inoculum	:	
Concentration	:	12 mg/l related to DOC (Dissolved Organic Carbon) related to
Contact time	:	7 day(s)
Degradation	:	100 % after 7 day(s)
Result	:	
Method	:	Standard coupled-units procedure usind DOC removal as parameter.
Test substance	:	p-Nitrophenol CASNO 100-02-7
Reliability	:	(2) valid with restrictions

Details lacking

29.02.2004 (6)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	>= 5.8 calculated
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	other TS
Method	:	This study preceeded development of OECD Test Guideline 203 but was conducted in a manner consistent with that guideline. Groups of bluegill fingerlings (mean length of 2.8 cm); fish were not fed 48 h prior to nor during the 96 hr exposure period. Groups of 10 fish were added to glass vessels containing 15 l water at 5 test concentrations (8.7, 5.6, 3.7, 2.4 and 1.6 mg/L PNP) dissolved in acetone. Both a negative control and an acetone-containing control group were also used. No aeration was performed during the test. Water temperature was maintained at 22+/-1%, with a pH ranging between 6.7-6.3. Dissolved oxygen ranged from 93% saturation at study start to 7% at study termination. Observations and mortality were checked every 24 hr. At the end of the study, test concentrations and observed mortality were converted to logarithms and probits, respectively, and analyzed by a least square regression method for determination of LC50 and CI at 24, 48, and 96 hr timepoints.
Result	:	All deaths occurred during the first 24 hr of the study, hence the LC50 and CI values for each of the study time points (24, 48, 96 hr) were the same, i.e. LC50 = 5.8 (3.7-9.2) mg/L. Mortality (%) observed at each concentration was: 100% @ 8.7mg/L, 10% @ 5.6 mg/L, and 0% @ 3.7 mg/L, 2.4 mg/L, 1.6 mg/L, untreated control and acetone control.
Test substance	:	Purity of 99%.
Reliability	:	(2) valid with restrictions This study was conducted prior to, but consistent with OECD Guideline # 203 and, US GLP guidelines effective in 1979 for nonclinical laboratory studies.Reduction in oxygen over time is not considered a factor in interpretation of results since all deaths (10%) occurred within first 24 hrs of study.
Flag	:	Critical study for SIDS endpoint

29.02.2004 (17)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static

Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	= 13 measured/nominal
EC50	:	>= 22 calculated
Analytical monitoring	:	no
Method	:	OECD Guide-line 202
Year	:	1980
GLP	:	no data
Test substance	:	other TS

Method : Methods used followed protocol as found in US EPA,1975 for Macroinvertebrate testing, which are consistent with OECD Guideline 202. D. magna, <24h old, were used as the tester strain. Culture water was reconstituted as outlined in US EPA, 1975 guidance, such that it contained a total hardness of 173+/-13 mg/l as CaCO3 and a pH of 8.0+/-0.2. Temperature was maintained at 22+/-1 degree C. A stock solution of the chemical in distilled water was prepared and used to provide a series of graded concentrations (reportedly 5-8) for testing. PNP was added to 500 mL diluent water in 2-L jars to prepare for each test solution. The 500 mL volume of test solution was divided into three 150-mL aliquots to provide triplicate exposures at each concentration. Five Daphnids were randomly placed in each test solution within 30 min of preparation. A negative control was also tested. Meaurements were taken to confirm dissolved oxygen concentration, pH, and temperature in the high, medium and low test concentrations. Observations were made at 24 and 48 hours of exposure and any mortalities were recorded. Mortality data were used to calculate an LC50 and CI using a moving average angle method.

Result :

LC50 (CI) values for 24 hr and 48 hrs were, respectively, 24 (22-26) mg/L and 22 (20-24) mg/L. ; The No Discernable Effect level was 13 mg/L. Dissolved oxygen concentrations ranged from 6.5-9.1 mg/L, pH values measured 7.4-9.4 units.

Test substance : Test compound purchased from commercial chemical supplier, hence technical grade PNP was likely used and had purity of 99%.

Reliability : (1) valid without restriction
GLP compliance was not stated in the article but adequate documentation can be assumed as this study was performed for the US EPA under contract no. 68-01-4646.

Flag : Critical study for SIDS endpoint

29.02.2004 (12)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC10	:	>= 8 calculated
EC50	:	>= 32 calculated
Limit test	:	

Analytical monitoring	:	no
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	
GLP	:	no data
Test substance	:	other TS
Method	:	Following test guidelines set by OECD, 1983 and German Umweltbundesamt, 1982. Experiments were incubated at 22+/-2 degrees C. at constant photosynthetically effective light intensity. Due to a distinct change of pH value caused by inclusion of PNP in sterilized double distilled water used as the diluent in this study, the pH of the stock solution was adjusted to pH 7 using NaOH. Experiments were performed by preparing two parallel dilution series in 300-ml Erlenmeyer flasks containing a saturated test chemical solution, medium and 5 ml algae suspension of approx. 10E4 cells/ml. Each Erlenmeyer flask was shaken 2-3 times per day and continuously illuminated from the side by two fluorescent lamps. After 0, 72 and 96 hrs, the cell growth of a 10-mm layer of cell suspensions from each test culture and from the controls was measured at 578 nm using a spectrophotometer. The extinction units were converted to cell numbers using a standard curve and the cell numbers determined using the Utermoehl method. The concentration-effect relationships were plotted on semilogarithmic paper and EC10 and EC50 values determined graphically. Concentrations of test material were determined based on its water solubility and a 2-fold dilution approach to which algal cells were added. The calculated relevant concentrations are 4.8, 9.6, 19.2, 32.4, 76.8 and 153.6 mg/L. These are not specifically given in the paper but were calculated in response to a request by EPA for concentrations.
Test substance	:	Commercial grade PNP, and thus with purity of 99%.
Reliability	:	(1) valid without restriction While not explicitly stated, the fact that this study was conducted according to national (Ger) and international (OECD) test guidelines it most likely was conducted consistent with or actually followed GLP guidance.
Flag	:	Critical study for SIDS endpoint

29.02.2004 (7)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 230 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	50
Vehicle	:	other
Doses	:	
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	1983
GLP	:	yes
Test substance	:	other TS
Method	:	Administered by gavage using propylene glycol as vehicle to 5 groups of rats (5 male and 5 female) given 70, 110, 171, 268 or 420 mg/kg/d; Clinical signs recorded 3X during first 8-hr after dosing and 2X daily for the remainder of the 14-d observation period. Body weights recorded on test days 0, 7 and 14. All survivors were necropsied on test day 15. Food and water administered ad libitum. LD50 and CI determined using method of Finney, DJ. 1971. Probit Analysis, Cambridge Univer. Press.
Result	:	LD50 +/- Confidence Limits (95%): 230 mg/kg (182-289 mg/kg); Deaths: 70 mg/kg (0/10), 110 mg/kg (0/10), 171 mg/kg (3/10), 268 mg/kg (8/10) and 420 mg/kg (8/10); Deaths all occurred within the first 8 hrs of dosing and exhibited the following clinical signs: convulsions, prostration and dyspnea prior to death; Clinical signs observed in survivors during the first three days after dosing included: tremors, ptosis, salivation and lethargy. No untoward effects were noted at necropsy of survivors.
Test substance	:	Technical grade purity of > 99%
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

29.02.2004 (21)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD0
Value	:	> 5000 mg/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	10
Vehicle	:	physiol. saline
Doses	:	
Method	:	OECD Guide-line 402 "Acute dermal Toxicity"
Year	:	1983
GLP	:	yes

Test substance	:	other TS
Method	:	One group of 5 male and 5 female rabbits were administered 5000 mg/kg/d test material on the shaved and abraded dermal surface. After administration the site was occluded and test material left in place for 24 hours. After test material removal, animals were observed for the remainder of the 14-d observation period. Clinical signs were recorded 3X during the first 8 hrs and 2X daily for the remainder of the study. Body weights were recorded on test days 0, 7 and 14. Necropsies were performed on all animals on test day 15. Food and water were administered ad libitum.
Result	:	No deaths occurred and no signs of systemic toxicity were seen during the study or at necropsy. Erythema and edema were observed during visual observations and at necropsy.
Test substance	:	Technical grade purity of > 99%
Reliability	:	(1) valid without restriction

29.02.2004 (22)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	13 weeks
Frequency of treatm.	:	Once daily throughout the exposure period
Post exposure period	:	None
Doses	:	0, 25, 70 and 140 mg/kg/d
Control group	:	yes, concurrent vehicle
NOAEL	:	= 25 mg/kg
LOAEL	:	= 70 mg/kg
Method	:	OECD Guide-line 408 "Subchronic Oral Toxicity - Rodent: 90-day Study"
Year	:	1989
GLP	:	yes
Test substance	:	other TS
Method	:	Groups of 20M and 20F S-D rats were administered 0, 25, 70 or 140 mg PNP/kg daily in distilled water for 13 weeks by gavage at a constant volume of 10 ml/kg. Dose levels were verified by spectrophotometric analysis. Mortality checks and signs of intoxication were made twice daily, and detailed clinical signs, individual body weights and food consumption recorded weekly. Pre and post study ophthalmoscopic examinations were also conducted on all animals available. At weeks 7 and 14 extensive hematology (RBC, RETIC, HGB, HCT, PLATELET, WBC, differential Leukocytes, and cell morphology) and serum chemistry (GLU, BUN, CREAT, AST, ALT, GGT, T PROT., ALBU, GLOB, CA, T BILI, PHOS, NA, POTAS, CL) parameters were conducted on blood

samples from 10 animals/sex/group. No urinalysis was performed. At termination brain, liver, kidney, spleen and testes with epididymides were weighed for all survivors and a full necropsy performed. A full set of approx. 40 tissues and organs (including gonads) were collected from all surviving animals and sections were examined microscopically from these tissues for the control and high dose animals. Microscopic examination of tissues was also performed on tissues of premature deaths exhibiting gross autopsy findings. Temperature, lighting and humidity were controlled throughout the study. Body weights and weight gains, food consumption, hematology and clinical chemistry parameters and organ weights (absolute and relative) were initially analyzed using Levine's test of homogeneity of variances. If nonhomogeneous, data were transformed and then analyzed via ANOVA ($p<0.05$). Dunnett's t-test (2-tail, $p<0.05$) was used to compare treated and control groups. Cumulative survival was assessed using the National Cancer Institute statistical package and analyzed for trend.

Result :

Early deaths were seen in groups of male and female rats given 70 and 140 mg/kg/d PNP. Total premature deaths observed in 0, 25, 70 and 140 mg/kg males were 0,0,1, 15, respectively; for females - 0,1,1,6, respectively; Several of these premature deaths (1-70 mg/kg male, 2 @ 140 mg/kg male, 3 @ 140 mg/kg female) died shortly after bleeding at wk 7, which likely exacerbated deaths, while 1 HD male was found to have died from gavage error. All other deaths at 70 mg/kg and 140 mg/kg were considered related to PNP exposure as they exhibited significant clinical signs of toxicity (pale appearance, languid behavior, prostration, wheezing and dyspnea), died shortly after dosing and exhibited moderate to severe congestive liver, kidney, lungs and adrenal cortex pathology (which correlated with necropsy findings) after microscopic examination; The presence of clinical signs of toxicity and absence of specific histopathological changes in these premature deaths suggests a relationship to acute pharmacologic/toxicologic effect. The single premature death observed in the LD female group was not considered treatment-related as there were no clinical signs observed, it did not die shortly after dosing (was found dead overnight) and had little in the way of organ congestion. Significant increases were observed in segmented neutrophils and absolute monocytes and eosinophil counts, as well as polychromasia of erythrocytes in 140 mg/kg animals of both sexes; these findings were considered of no toxicological significance. No treatment-related effects were observed in clinical signs, body weights, food consumption, ophthalmoscopic examination, organ weights or histopathology of survivors. Specifically, no effects were observed on gonads in this study. A NOEL was established as 25 mg/kg/d.

Test substance : Purity of 99%
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
29.02.2004 (20)

Type	:	Sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	4 weeks
Frequency of treatm.	:	6 hr/d, 5 days/week
Post exposure period	:	none
Doses	:	0, 1, 5, and 30 mg/m3
Control group	:	yes
NOAEL	:	= 5 mg/m³
LOAEL	:	= 30 mg/m³
Method	:	OECD Guide-line 412 "Repeated Dose Inhalation Toxicity: 28-day or 14-day Study"
Year	:	
GLP	:	yes
Test substance	:	other TS

Method :

Groups of 15 male and 15 females S-D rats were exposed to target concentrations of 0, 1, 5 or 30 mg/m3 of PNP dust via whole body exposure in 1000 L glass and stainless steel chambers. Chamber concentrations were generated via use of a Wright dust feed and determined 3X daily by gravimetric analysis. Particle size determinations were measured weekly. Food and water were available ad libitum at all times other than during exposure. Temperature and humidity, as well as light:dark cycle were controlled. Animals were observed twice daily for mortality and signs of toxicity. Each animal was carfully examined and weighed weekly. Hemoglobin and methemoglobin concentrations were determined by orbital sinus during week 2. Ophthalmic exams were conducted just prior to terminal sacrifice on all animals. The following hematology (RBC, HCT, HGB,PLATELETS, RBC morph, and total and differential leukocyte counts, and clotting time) and blood chemistry (ALT, AST, BUN, TOT BILI, GLU, LD, CHOL, NA, POTAS, CA, CL, PROT, ALBU, GLOB) were evaluated after 4 weeks. No urinalysis was performed. Complete necropsies were conducted on all animals on test. The following organ weights were recorded: lungs, liver, kidneys, brain, heart, adrenals, spleen and testes with epididymides. Thymus wt was not recorded. Histopathological examinations were conducted on approximately 40 tissues and organs, and all gross lesions observed at necropsy, on all high dose and control animals. Clinical pathology, hematology, weekly body weights and weight gains, organ weights and weight ratios of control groups were compared statistically to treated groups of the same sex. Box test was used to determine homogeneity of variances followed by a 1-way classification by ANOVA if variances were homogeneous or use of rank transformation if nonhomogeneous. If found significant ($p<0.05$) Dunnett's t-test was used to compare groups ($p<0.05$).

Result :

Mean gravimetric chamber concentrations were 1.09, 5.27, and 29.2 mg/m3. MMD ranged from 5.4-6.9 u. Prestudy analysis indicated that the PNP dust was homogeneously distributed in the stainless steel chamber. No deaths occurred during the study. Except for dose-related yellow staining attributed to

test material, no abnormal physical observations were noted. Ophthalmoscopic examinations revealed 11 cases of diffuse anterior capsular cataracts only in HD males and females. Corneal keratitis sicca (inflammation and drying of the cornea and conjuctiva) was noted in 3 HD animals. Periodic changes in body weights were seen inconsistently and in opposite directions for each sex and thus not considered tretment-related. No consistent, dose-related effect was noted in METH values, while some very slight changes in HGB and HCT were seen in HD males. The relationship of these effects to PNP treatment is unclear. No treatment-related effects were seen in other hematologic or clinical chemistry parameters. No gross or microscopic pathological effects or organ weight changes were noted that were attributed to PNP. No effects on the gonads was observed. A NOEL was established as 5 mg/m3.

Test substance : Purity of 99 %.
Reliability : (1) valid without restriction
29.02.2004 (18)

Type :
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : 4 weeks
Frequency of treatm. : once daily for the entire test period
Post exposure period : none
Doses : 0, 1, 10, 50, and 100 mg/kg
Control group : yes, concurrent vehicle
NOAEL : = 50 mg/kg
LOAEL : = 100 mg/kg
Method : other
Year : 1989
GLP : yes
Test substance : other TS

Method : Groups of 5 male and 5 female S-D rats were administered PNP in distilled water by gavage at doses of 0, 1, 10, 50 and 100 mg/kg at a constant volume of 10 ml/kg. Daily clinical signs were recorded and individual body weights and food consumption were taken weekly for all animals. Hematological (HGB, HCT, RBC, TOT /DIFF LEUKO, MET HGB) and clinical pathological (BUN, GLU, CREAT, ALT, ATS, T PROT, ALBU, GLOB, T BILI, PHOS, NA, K, CL) parameters were measured prior to study termination after 4 weeks. Gross necropsy examinations were conducted at the terminal sacrifice and brain, liver, kidneys, spleen and testes with epididymides were trimmed and weighed. Collected tissues (approx. 40/animal) were preserved and gross lesions, kidneys, livers and spleen were prepared from all animals and examined microscopically. Dosing solutions were analyzed by spectrophotometric means for stablity and concentration.

Result :

Analysis of dosing solutions indicated stability and accuracy. One female rat at the 100 mg/kg dose level died shortly after bleeding followed by dosing and is likely

treatment-related. Mean body weights and food consumption in treated groups were comparable to control values. No changes were observed in hematology or clinical chemistry values between treated and control groups. No clinical signs of toxicity were observed in survivors. Organ weights, necropsy findings and microscopic examination of treated rats were similar to controls.

Test substance :

p-Nitrophenol (CASNO 100-02-7), purity 99.1%

Conclusion :

This study was a range-finding study to set dose levels for study no. HL-88-372. As such, no statistical treatment of data was ascertained.

Reliability : (2) valid with restrictions
29.02.2004 (19)

Type : Chronic
Species : mouse
Sex : male/female
Strain : Swiss Webster
Route of admin. : dermal
Exposure period : 18 months
Frequency of treatm. : 3 days per week
Post exposure period : none
Doses : 40, 80 or 160 mg/kg in acetone
Control group : yes, concurrent vehicle
NOAEL : = 160 mg/kg bw

Method :

Sixty Swiss-Webster mice of each sex received 0, 40, 80, or 160 mg/kg p-nitrophenol in 100 microliters acetone applied directly to the interscapular skin three times per week (Monday, Wednesday, and Friday; excluding holidays) for 78 weeks. Fur in the area of skin receiving the dose application was clipped weekly. Doses selected for the 18-month studies were based on the survival and histopathologic lesions from 13-week studies conducted at the Gulf South Research Institute. (unpublished data). The study conduct followed the NTP statement of work.

Dose analyses of p-nitrophenol in acetone were performed at approximately 2-month intervals by the study laboratory using flame-ionization gas chromatography with n-undecanol as internal standard. Dose formulations were within 10% of the desired level during the entire study

Mice were examined twice daily for mortality, changes in appearance or behavior, and signs of toxicologic or pharmacologic effects. Clinical findings were recorded weekly for the first 13 weeks, then at 4-week intervals thereafter until the end o f the study. Body weights were recorded weekly for the first 12 weeks, then every 4 weeks until the end of the study. Complete necropsies were performed on all mice. During necropsy all organs and tissues were examined for gross lesions. Complete histopathologic examination was performed on all mice. Tissues selected for microscopic examination were preserved in 10% neutral buffered formalin. To prepare the tissue for microscopic examination, the preserved tissue was embedded in paraffin, sectioned 4 to 6 pm thick, and stained with hematoxylin and eosin. The NTP complete list of tissues was examined microscopically.

Result	:	Survival of dosed male and female mice was similar to that of the controls. (Survival of 40 mg/kg males was significantly lower than that of controls but this was not considered to be related to chemical administration) There were relatively few deaths during the first 60 weeks o f the study, and thereafter, survival began to decrease abruptly for all dosed and control groups. Body weights of dosed mice were similar to controls throughout the study. No statistically significant or biologically noteworthy changes occurred in the incidences of nonneoplastic lesions at any site. There we no compound-related increases in any neoplasm. A full description of the results is available in NTP TR 417 which can be found on the NTP website at http://ntp-server.niehs.nih.gov/htdocs/LT-Studies/TR417.html
Test substance	:	p-Nitrophenol CASNO 100-02-7 > 97% purity
Conclusion	:	Under the conditions of these 18-month dermal studies there was no evidence of carcinogenic activity or target organ effects other than the skin in male or female Swiss-Webster mice receiving 40, 80, or 160 mg/kg p-nitrophenol.
Reliability	:	(1) valid without restriction NTP Statement of Work study under GLP's, peer-reviewed and publically available.

29.02.2004 (15)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium strains TA100, TA98, TA1535 and TA1537
Test concentration	:	0, 10, 33, 100, 166, 333, 666, 1000 ug/plate
Cycotoxic concentr.	:	1000 ug/plate (TA100)
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471
Year	:	1983
GLP	:	yes
Test substance	:	other TS
Method	:	Methodology used by NTP based on Ames test plate incorporation assay and consistent with OECD 471. All tests were run in duplicate and three plates were assayed at each dosage for each run both with and without metabolic activation; S9 obtained from male S-D rats injected with Arochlor 1254 (500 mg/ml) five days before they were killed; all tester strains obtained originally from B. Ames; the high dose was designed to produce toxicity (reduced background lawn or solubility limits; sterile DSMO was used as the solvent; negative (solvent) and positive controls (2-aminoanthracene, 4-nitro-o-phenylenediamine, sodium azide and 9-aminoacridine) used were appropriate to detect mutagenicity with or without metabolic activation in each of the 4 tester strains used. A positive response was detected

if a reproducible, dose related increase (>2X) was seen in revertant colonies according to a model described by Margolin et al 1981.

Remark :

This result is supported by a secondary tier Drosophila Sex-Linked Recessive Lethal assay; no mutagenicity was observed after either oral or injection dosing up to lethal doses by each route in this same NCI/NTP program National Toxicology Program (NTP). 1994. Toxicology and carcinogenesis studies of p-nitrophenol in Swiss-webster mice (dermal studies). Technical Report Series No. 417, US Dept. HHS, PHS, National Institutes of Health.

This result is also supported by a 1990 report that PNP elicited no mutagenic activity when tested in a CHO-HGPRT forward mutation assay in mammalian cells. Oberly, TJ, Rexroat, MA, Beusey, BJ, Richardson, KK, Michaelis, KC. 1990. An evaluation of the CHO/HGPRT mutation assay involving suspension culture and soft agar cloning: Results for 33 chemicals. Environ Mol Mutagen 16(4):260-271.

Result :

No increase in revertants were observed with or without metabolic activation in any of the 4 tester strains.

Test substance : Purity = 99%.

Reliability : (1) valid without restriction
While no statistical methods were used, none were needed to visually inspect and render a conclusion of no increases observed in revertants in any tester strain; further, these findings are consistent with other literature citations using similar methodology

Flag : Critical study for SIDS endpoint

29.02.2004 (10)

Type : Chromosomal aberration test
System of testing : Chinese Hamster Ovary cell culture
Test concentration : 100 to 2500 ug/ml
Cycotoxic concentr. : not stated
Metabolic activation : with and without
Result : positive
Method : other
Year :
GLP : yes
Test substance : other TS

Method : Study performed under auspices of US NTP program. Doses were based on a preliminary test of cell survival 24 hr after treatment. Cells were collected 10.5 h after treatment by mitotic shaking-off. Slides stained with Giemsa and coded. 100 cells were scored from each of the 3 highest dose groups having sufficient metaphases for analysis (cells with 19-23 metaphases chosen); Positive control groups treated with triethylenemelamine, mitomycin C or Cyclophosphamide), solvent control also used.. Aberrations were typed and recorded separately but analyzed grouped into categories of simple (breaks and terminal deletions), complex (rearrangements and exchanges) and other (i.e pulverized chromosomes). Gaps and endoreduplications were recorded but not included in totals. Aberrations in polyploid cells were not scored. Linear regression of the percentage of cells

with aberrations vs. the log-dose was used as the test for trend. A binomial sampling assumption was used and data were analyzed according to the method of Margolin et al Environ Mutag 8:183 (1981). P values were adjusted by Dunnett's method to take multiple dose comparisons into account.

Remark :

In a concurrent study PNP was negative for SCE induction up to doses that caused severe cell cycle delay (25 ug/ml -S9; 1700 ug/ml +S9). National Toxicology Program (NTP). 1994. Toxicology and carcinogenesis studies of p-nitrophenol in Swiss-webster mice (dermal studies). Technical Report Series No. 417, US Dept. HHS, PHS, National Institutes of Health.

Result :

No treatment-related increase in the frequency of structural aberration were noted up to severe cytotoxic levels (>750 ug/ml -S9; Reproducible , dose-related and significant increases in cells with structural chromosomal aberrations were seen at test levels of 1500 to 2000 ug/ml +S9 that induced severe cell cycle delay.

Test substance : Purity of 99 %.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
29.02.2004 (5)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type : Two generation study
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : dermal
Exposure period : F0: males - 113 doses; females - 118 doses; F1: males - 190 doses; females - 180 doses
Frequency of treatm. : once per day, 5 days per week
Premating exposure period
Male : 140 days (100 doses)
Female : 140 days (100 doses)
Duration of test : Through prebreeding, breeding ,gestation, lactation and development through two full generations (1 litter per generation), F2 pups observed through 30 days postweaning.
No. of generation studies :
Doses : 50, 100, and 250 mg/kg/day
Control group : yes, concurrent vehicle
NOAEL parental : 250 mg/kg bw
NOAEL F1 offspring : 250 mg/kg bw
NOAEL F2 offspring : 250 mg/kg bw
Method : other
Year : 1985

GLP : yes
Test substance : other TS

Method : 5-Week old Charles River CD rats began treatment, consisting of 120 female and 60 male rats housed in wire mesh caging. Humidity, temperature and light:dark cycle were controled throughout the study. Water and food were available ad libitum. After random assignment, each of the five test groups began the study (Fo generation) with 24 females and 12 male rats per group. All rats were clipped free of hair along the dorsal body line and reshaved as necessary to allow good dermal contact with the test agent. Dosing periods were lengthened over the periods recommended by EPA guidelines to compensate for a 5-day per week dosing period in this study. Test agents were applied dermally using appropriate-sized syringes, once daily, 5 days /week. Animals were individually weighed at the beginning of each study and dose levels adjusted. F0 animals were treated for the first 140 days of the study (100 applications each). Thereafter, one half of the females in each group were paired with corresponding males until either positive mating was achieved (presence of sperm plug and confirmed by vaginal smear) or it became evident that the pair would not mate. In the latter cases additional cohousing occurred until it became apparent that no further mating would ensue. After successful mating, males and females were separated; F0 males were held until all mating ceased, at which time they were sacrificed and testes, epididymis and skin sections were taken for histopathologic evaluation. Dosing of F0 females continued through the breeding, gestation and lactation periods. Females dosed during gestation were based on the last premating weight. Approximately 21 days after birth, the F1 generation was weaned and F0 females sacrified with their ovaries, uterus and skin sections taken for histopathologic examination. 13 males and 26 females from the F1 generation were randomly selected for continued dosing and breeding in a manner similar to the F0 generation. Application of test materials continued over the next 168 days (120 applications each). Following this period, the F1 rats were mated in a procedure corresponding to the mating of the F0 parental animals. Five males and 5 female pups from the F1 generation were selected at weaning for complete necropsy exam. An additional 5 F2 males and 5 F2 females from each group were randomly selected and retained in wire cages for 30 days after weaning. Dosing of all F1 rats continued throughout breeding, gestation, lacatation and until 30 days after all F2 rats had been weaned. Thereafter, all F1 rats and remaining F2 rats were submitted for complete necropsy. All animals dying spontaneously during the course of the study were submitted for necropsy. All rats which underwent necropsy were subjected to histopathological assessment of the following tissues and organs: (brain, spinal cord, eye, salivary gland, heart, thymus, thyroid, lungs, bronchi, esophagus, stomach, small intestine, large intestine, pancreas, adrenal glands, kidneys, liver, testes, epididymis, urinary bladder, male accessary glands, ovaries, corpus uteri, cervix uteri,

spleen, lymph nodes, sernum, femur, skeletal muscle, mammary gland, treated skin and untreated skin. Organ weights were recorded for scheduled sacrifies from F1 and F2 animals: liver, kidneys, heart, gonads (F0 males also), and brain.

Observations for toxic signs, breeding and nesting behavior were recorded daily for all animals. Weights of all dosed rats were recorded weekly. Breeding and litter observations included: litter size, individual pup weights and viability at birth and on days 4, 7, 14, and at weaning. The following indices were calculated to assess reproductive success: fertility (no. of pregnancies/no. mated) gestation (% of pregnancies resulting in birth of live litters), viability (pups surviving at least to day 4 of life) and lactation (pups surviving at least to day 21 of life). Group-wise statistical ($p < 0.05$) comparisons were made of body weights, absolute and relative organ weights.

The High dose (250 mg/kg/d) was selected based on a range-find study indicating this level to be 1/4 LD50 dermally, and would allow sufficient survival; both an ethanol vehicle (used at 500 mg/ml) control group (0.5 ml/kg/d) and a saline control group (0.5 ml/kg/d) were also evaluated concomittantly. Multigeneration study methodology was modified (dosing took place 5 d/wk rather than 7 d/wk) from test guidelines recommended in TFX Collins Handbook on Teratology, Vol. IV, Chapter 7: Multigeneration Reproduction Studies. 1978.

Result :

All F0 and F1 rats dosed dermally with PNP or ethanol exhibited a pattern of dermal irritation consisting of varying degrees of erythema, scaling, scabbing and cracking ; some degree of dose-response was noted in PNP-treated groups. No treatment-related mortality was observed in either the F0 or F1 parental generation, and no effects of treatment were noted in body weights in these groups. No evidence of effects in mating, pregnancy, behavior,and growth were found in parents or subsequent F1 and F2 generations.All group-wise comparison of organ weights, including gonads, were unremarkable. No evidence of histopathologic alterations was seen in any tissue examined, including the gonads.

Test substance : Purity of test substance used - 99.1%

Reliability : (1) valid without restriction
Study sufficiently adequate to be accepted to fulfill US EPA pesticide reregistration requirement for reproductive toxicity endpoint.

Flag : Critical study for SIDS endpoint

29.02.2004 (1)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : gavage

Exposure period	:	gd 6 to 16
Frequency of treatm.	:	daily
Duration of test	:	
Doses	:	1.4, 13.8 or 27.6 mg/kg-day
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	= 13.8 mg/kg bw
NOAEL teratogen.	:	= 27.6 mg/kg bw
Result	:	not a developental toxin in the rat
Method	:	
Year	:	
GLP	:	no data
Test substance	:	

Method :

Test material, in propylene glycol solution, was administered by gavage to groups of 20 pre-mated female Sprague-Dawley rats at dose levels of 0, 1.4, 13.8 or 27.6 mg/kg-day from days 6 through 16 of gestation. A positive control group (aspirin, 250 mg/kg-day) was included in this study. Rats were sacrificed prior to delivery and the products of conception were examined for viability, morphology and other standard fetal parameters.

Result :

Decreased maternal body weight (12%) and body weight gain (45%) were observed during the dosing period at the high-dose level of 27.6 mg/kg-day. Treatment-related effects on mortality, clinical signs, food consumption or cesarean parameters were not reported. Food consumption was not measured.
Based on decreased body weight and body weight gain the maternal LOEL is judged to be 27.6 mg/kg-day. The maternal NOEL was found to be 13.8 mg/kg/day. The developmental NOEL was found to be 27.6 mg/kg-day and a developmental LOAEL was not found.

Treatment-related developmental toxicity was not observed; however, the small number of litters (10) available for examination at the high dose level and the lack of some experimental details in the report reduce reliability of the results. A developmental NOEL of 27.6 mg/kg-day can be assigned. A developmental LOAEL was not established in the study.

Test substance :

p-Nitrophenol (CASNO 100-02-7), purity 99.1%

Conclusion :

It is concluded that the test material did not demonstrate any developmental toxicity even at doses associated with clear maternal toxicity.

Reliability : (2) valid with restrictions

Although the number of litters was sub-optimal, and some experimental details are missing, the lack of any adverse effects on developmental parameters in animals where maternal weigh-loss was reported during administration of test material is a strong indication that the test material is not a developmental toxin. The study is assigned a reliability score of 2 because of it lacks details.

Flag : Critical study for SIDS endpoint

29.02.2004 (2)

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